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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/360,934	07/26/1999	ANTONELLO COVACCI	CHIR-0158	4878

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/09/2003

35

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/360,934	Covacci et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 1, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *40, 54, 61-65, 72-75, 82-86, 93-96, and 98-101* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *40, 54, 61-65, 72-75, 82-86, 93-96, and 98-101* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *34.*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 04/01/03 (paper no. 32) has been entered.

Applicants' Amendment

2) Acknowledgment is made of amendment filed 04/01/03 (paper no. 33) in response to the final rejection mailed 12/18/02 (paper no. 31).

Status of Claims

3) Claims 58-60, 69-71, 79-81, 90-92 and 97 have been canceled via the amendment filed 04/01/03.

Claims 40, 63, 74, 84, 95 and 99 have been amended via the amendment filed 04/01/03. The requested amendment to claims 55 and 76 are NOT entered, since these claims have already been canceled via a previous amendment filed 09/20/02 (paper no. 30).

Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are pending and are under examination.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' information disclosure statement filed 04/01/03 (paper no. 34). The information referred to therein has been considered and a signed copy of the same is attached to this Office Action (paper no. 35).

Priority

5) This application is a Divisional application of SN 08/466,662 filed 06/06/95, *now US patent 6,130,059*, which is a Divisional application of SN 08/256,848, filed 10/21/94, now abandoned, which is a national stage application of PCT/EP93/00472, filed 03/02/93 and PCT/EP93/00158, filed 01/25/93. The instant application claims priority benefit to the Italian application, SN FI 92A000052, filed 03/02/92.

Prior Citation of Title 35 Sections

6) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

7) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Maintained

8) The objection to the informal drawings made by the previous Examiner of record in paragraphs 3 and 4 of the Office Action mailed 12/18/02 (paper no. 31) is maintained for reasons set forth therein. Applicants are asked to note the changes effected 03 May 2001, particularly the changes to the 'Timing of Corrections':

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85; 1097 O.G. 36

New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the "Notice of Allowability" (PTOL-37 or PTO-37). If delayed, the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability" to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 C.F.R 1.136(a) for filing the corrected drawings (but not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed

changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, Applicant must arrange to have an acceptable correction re-submitted within the original three month period to avoid the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

Specification - Informalities

9) The specification is objected to for the following reasons:

(a) The amendment introduced to the first paragraph of the specification via the paper filed 07/26/99 (paper no. 2) does not accurately reflect the current issued status of the earlier filed application(s) as indicated above in italicized letters under 'Priority'. Amendment to the first paragraph of the specification is needed to reflect this.

(b) The use of the trademarks in the instant specification has been noted in this application. For example, see page 39, last paragraph: "Tween 80 "; "Span 85" and "Squalene". Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(c) On page 61, lines 4-6, the address of the American Type Culture Collection is incorrect. Effective 23 March 1998, ATCC has a new address: 10801 University Boulevard, Manassas, VA 20110-2209. Amendment to the specification is suggested to reflect this. It is suggested that Applicants examine the whole specification to make similar correction to the address, wherever it appears.

Double Patenting Rejection(s)

10) The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

Claims 40, 54, 63-65, 74, 75, 84-85, 95, 96 and 98-101 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38, 44, 45 and 46 of the co-pending application SN 09/921,157. Although the conflicting claims are not identical, they are not patentably distinct from each other because the product(s) claimed in the instant claims are cytotoxin polypeptide of SEQ ID NO: 3 or polypeptides comprising a fragment of the recited size. The limitation 'recombinant' in some claims merely represents a process limitation.

Rejection(s) Moot

11) The rejection of claims 58, 59 and 78-80 made/maintained by the previous Examiner of record on paragraph 3 of the Office Action mailed 12/18/02 (paper no. 31) under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

12) The rejection of claims 58 and 79 made by the previous Examiner of record on page 4 of the Office Action mailed 12/18/02 (paper no. 31) under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

13) The rejection of claims 59 and 80 made by the previous Examiner of record on page 4 of the Office Action mailed 12/18/02 (paper no. 31) under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

14) The rejection of claims 58-60, 69-71, 79-81, 90-92 and 97 made by the previous Examiner of record on page 8 of the Office Action mailed 12/18/02 (paper no. 31) under 35 U.S.C. § 102(e) as being anticipated by, or alternatively, 35 U.S.C. § 103(a), as being unpatentable over Cover *et al.* (US 6,054,132), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

15) The rejection of claims 95 and 96 made by the previous Examiner of record on page 6 of the Office Action mailed 12/18/02 (paper no. 31) under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn in light of Applicants' amendment to the claims and./r the base claims.

16) The rejection of claims 40, 54, 61-65, 74, 75, 82-86, 93-96 and 98-101 made by the previous Examiner of record on page 8 of the Office Action mailed 12/18/02 (paper no. 31) under 35 U.S.C. § 102(e) as being anticipated by, or alternatively, 35 U.S.C. § 103(a), as being unpatentable over Cover *et al.* (US 6,054,132), is withdrawn. A modified rejection is made below.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

17) Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 40, 54, 74, 75 and 98 are vague in the recitation "SEQ ID NO: 3" without reciting that the SEQ ID NO: 3 represents an amino acid sequence. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with --the amino acid sequence of SEQ ID NO: 3--.

(b) Claim 63, 64, 65, 84-86 and 99-101 are vague in the recitation "SEQ ID NO: 2" without reciting that the SEQ ID NO: 2 represents a polynucleotide sequence. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with --the nucleotide sequence of SEQ ID NO: 2--.

(c) Claims 40, 74, 84, 95 and 99 are vague and/or confusing in the recitation: "exhibits substantially no toxicity, or a substantially reduced toxicity", because it is unclear what degree of toxicity qualifies as substantially no toxicity or substantially reduced toxicity. The specification does not appear to provide a standard for ascertaining the requisite degree of toxicity that qualifies as

"substantially no toxicity" and "substantially reduced toxicity". The term "substantially" is a relative term which renders the metes and bounds of the claims indeterminate. The toxicity is not specified, and therefore encompasses cytotoxicity, endotoxicity, exotoxicity, cell-vacuolizing toxicity, or any other type of general toxicity. What exact toxicity and what degree of toxicity are encompassed in the limitation: 'substantially no toxicity' or 'substantially reduced toxicity', is not understood. The terms 'substantially no toxicity' and 'substantially reduced toxicity' are not specifically defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and therefore, one of ordinary skill in the art would not be reasonably appraised of the scope of the claims.

(d) Claim 95 is confusing in the recitation "formulation of vacuoles", because it is unclear what is encompassed in 'formulation'. It is not clear how does this limitation differ from the limitation in claims 96 and 99: "formation of vacuoles". Clarification/correction is requested.

(e) Claims 95 and 99 are indefinite, confusing and/or internally inconsistent in that part (i) recites that the cytotoxin causes the formation of vacuoles in eukaryotic cells, indicating that the claimed polypeptide is 'cytotoxic', yet part (ii) of the claims recites that the polypeptide 'exhibits substantially no toxicity, or substantially reduced toxicity'. It is unclear how a polypeptide can be toxic and substantially non-toxic at the same time. Furthermore, it is unclear whether or not the toxicity encompassed in part (i) of the claims is included or excluded from the scope of the 'toxicity' recited in part (ii) of the claims.

(f) Claims 61, 62, 72, 73, 82, 83, 93 and 94 are vague, confusing and/or incorrect in the recitation "polypeptide comprising at least .... kDa". The 'kDa' is not a structural element of the polypeptide to be comprised within the polypeptide, but represents a property, i.e., molecular weight, of a polypeptide. In order to distinctly claim the subject matter and for clarity, it is suggested that Applicants replace the recitation with --polypeptide having a molecular weight of at least ... kDa--.

(g) Claims 96, 98, 100 and 1001, which depend directly or indirectly from claim 95, are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, because of the indefiniteness or vagueness, identified above in the base claim.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

18) Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are rejected under 35 U.S.C. § 112,

first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 84 now includes the new limitation: " .....immunologically identifiable by antibodies which react specifically with the polypeptide expressed by the nucleotide sequence of SEQ ID NO: 2". Claims 40, 63, 74, 95 and 99 include the new limitation: ".... is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3". Applicants state that these limitations are supported in the specification at page 14, lines 21-30. However, this part of the specification pointed to by Applicants does not provide descriptive support for a recombinant polypeptide of the amino acid sequence of SEQ ID NO: 3, or a fragment thereof of the recited size that is immunologically identifiable by antibodies which react specifically with *Helicobacter pylori* cytotoxin **and** which at the same time exhibits substantially no toxicity or substantially reduced toxicity, as recited. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or invited to point to specific pages and line numbers in the specification where support for such recitations can be found.

19) Claims 40, 54, 61-65, 72-75, 82-85, 93-96 and 98-101 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Instant claims encompass a recombinant polypeptide, or an immunogenic recombinant polypeptide comprising "at least ten contiguous amino acids" or "at least fifteen contiguous amino acids" of the polypeptide of SEQ ID NO: 3; "at least 5 contiguous amino acids expressed from at least 15 contiguous nucleotides of SEQ D NO: 2", "at least 30 contiguous nucleotides of SEQ ID NO: 2", or "at least 45 contiguous nucleotides of SEQ ID NO: 2" of *H. pylori*. The at least five-,

ten-, or 15-mer polypeptide does not exist independent of its function, but is required to have the capacity to be 'immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3' **and** the ability to 'exhibit substantially no toxicity, or substantially reduced toxicity'. The specification intends diagnostic, prophylactic or therapeutic applications for the claimed polypeptide. Claims do not identify the five, ten or 15 amino acid-long polypeptides. Claims do not identify the precise type of toxicity. The polypeptide claimed in claims 95, 96 and 98-101 is a very complex cytotoxin polypeptide or a fragment thereof, which is recited in part (i) of claim 95 as being cytotoxic due to its ability to cause the formulation of vacuoles in eukaryotic cells, but at the same time is recited in part (b) as exhibiting 'substantially no toxicity, or substantially reduced toxicity' and is also concurrently required to have the capacity to be immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3. A review of the instant specification shows that Applicants were not in possession of these polypeptide fragments having all the recited or required properties. Instant claims recite insufficient relevant identifying structural characteristics of the claimed fragment(s) of the *H. pylori* cytotoxin antigen. The instant specification provides inadequate written description to allow one skilled in the art to predictably determine the structural composition of the fragment(s). The precise structural composition of the claimed cytotoxin polypeptide comprising at least 10, 15 or 5 amino acids is not adequately described such that one of ordinary skill in the art could produce such cytotoxin polypeptide fragments, which exhibit no substantially toxicity, or a substantially reduced toxicity **and** which have the capacity to be 'immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3' and/or the ability to cause the formulation of vacuoles in eukaryotic cells. There is a lack of written description as to which specific 5, 10 or 15 contiguous amino acid residues of the claimed cytotoxin antigen are encompassed in the claimed polypeptide fragment. It is uncertain whether retention of any 5, 10 or 15 contiguous amino acid residues from any part of the cytotoxin antigen of SEQ ID NO: 3 (i.e., terminal or central parts, or somewhere in between) would yield a polypeptide that would have the required capacity to be 'immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3' **and** the capacity to exhibit substantially no toxicity, or substantially reduced toxicity and/or the ability to cause the

formulation of vacuoles in eukaryotic cells. Furthermore, in order to be immunologically identifiable with an antibody that is 'specific' to *Helicobacter pylori* cytotoxin of SEQ ID NO: 3, the claimed polypeptide must be unique to *Helicobacter pylori* cytotoxin and must not be shared by other microbial or non-microbial antigens. A review of the specification shows that Applicants have not described such polypeptide fragments that specifically react with antibodies specific to *Helicobacter pylori* cytotoxin of SEQ ID NO: 3. The art, for example, indicates that an at least five amino acid-long fragment of the instantly recited SEQ ID NO: 3, AFFTT, is not specific or unique to *Helicobacter pylori* cytotoxin, but is shared by a non-*Helicobacter pylori* cytotoxin protein, for example, a sodium channel protein of *Drosophila*. See Table III of Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 - Applicants' IDS). Further added to this, is the conformational complexity of the epitopes of *Helicobacter pylori* cytotoxin (see abstract of Manetti *et al. Infect. Immun.* 63: 4476-4480, November 1995, already of record). Given these, one of skill in the art cannot produce immunologically identifiable at least five-mer, ten-mer or 15-mer cytotoxin polypeptides that are *Helicobacter pylori* cytotoxin-specific, without undue experimentation. The precise structure or relevant identifying characteristics of at least 5-mer, 10-mer or 15-mer cytotoxin polypeptide as claimed, wherein the polypeptide has the recited functional properties, can only be determined empirically by actually making every polypeptide that is encompassed in the claims and testing them. In view of the level of knowledge and skill in the art, the art-disclosed epitopic non-specificity and the art-recognized functional unpredictability, one skilled in the art would not recognize from the instant disclosure that Applicants were in possession of the recited cytotoxin fragments having the recited size and properties. See *Written Description Requirement* published in *Federal Register*, Vol. 66, No. 4, Friday, 05 January 2001, Notices, p. 1099-1111. The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The claimed polypeptide species have specific biological properties dictated by the structure of the polypeptide and the corresponding structure of the structural gene sequence which encodes it. There has to be some nexus between the structure of the polypeptide sequence and the function of such a

polypeptide. However, the function cannot be predicted from the modification or truncation of the structure of the recited polypeptide, SEQ ID NO: 3. Applicants have not shown that truncation of the polypeptide of SEQ ID NO: 3 to a five-mer, ten-mer or fifteen-mer size would automatically predict the production of polypeptides of *H. pylori* having all the required functions. The specification fails to teach the structure or precise relevant identifying characteristics of a representative number of at least 5-mer, 10-mer or 15-mer polypeptide species from SEQ ID NO: 3, sufficient to allow one skilled in the art to determine that inventors had possession of the invention as claimed. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating it. See *Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)* and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.* See Written Description Requirement, *Federal Register*, vol. 66, no. 4, Notices, pp. 1099-1111, 05 January 2001). Since which at least 5-mer, 10-mer or 15-mer polypeptide fragment of SEQ ID NO: 3 would retain *H. pylori* cytotoxin-specific immunological identifiability is neither disclosed, nor could be predicted, and since the precise epitopes on the cytotoxin polypeptide responsible for immunological reactivity with a specific antibody are not known or identified, one of ordinary skill would be forced into experimentation that is undue. *Vas-Cath Inc. V. Mathukar, 19 USPQ2d 1111* states that Applicant "must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, is for purposes of the 'written description' inquiry, whatever is now claimed." See page 1117. Therefore, the claims are viewed as not meeting the written description provision of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 102

20) Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are rejected under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 6,054,132, filed 02/26/1992 - already of record).

The limitation "toxicity" in this rejection is interpreted as encompassing toxicity due to endotoxin. It is noted that the limitation "toxicity" encompasses general toxicity. It is further noted that the transitional recitation "comprising" is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* ('132) disclosed an antigenic polypeptide of a cell vacuolating toxin (i.e., cytotoxin) of *Helicobacter pylori* which is recombinantly or synthetically produced, and a composition comprising the same (see column 2, lines 25-58). The polypeptide comprises a 23 amino acid-long N terminus of the toxin antigen, i.e., SEQ ID NO: 1, and is obtained from the purified toxin (see column 10, lines 2--4; and first sequence in columns 17 and 18 under Sequence Listing). The 23 amino acid-long antigenic portion of the polypeptide of the prior art has 100% sequence identity with a 23 amino acid-long contiguous portion that stretches between positions 34-56 of the instantly recited SEQ ID NO: 3. The antigenic polypeptide is present along with water, phosphate buffered saline or an adjuvant (see column 18, third paragraph; column 17, second paragraph; and column 16, lines 45-50). The polypeptide has a molecular weight of 87,000, or 972,000 daltons (see column 2, seventh full paragraph). That the polypeptide of the prior art comprising the 23 amino acid-long antigenic portion, obtained from a purified toxin, is pure enough to be of substantially no endotoxicity, or of substantially reduced LPS-related toxicity, and that it is long enough to be immunologically identifiable by antibodies specific to the amino acid sequence of SEQ ID NO: 3 are inherent from the teachings of Cover *et al.* ('132). Given that the structural elements of the instant claims are met by the prior art antigenic polypeptide, the immunological identifiability by antibodies specifically reactive with the amino acid sequence of SEQ ID NO: 3 and the exhibition of substantially no toxicity or of substantially reduced toxicity, including cytotoxicity, are viewed as the inherent properties inseparable from the antigenic polypeptide taught by Cover *et al.* ('132).

Furthermore, the term "recombinant" and/or "expressed from ..... nucleotides of SEQ ID NO: 2" in some of the claims represent process limitations. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a

product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art antigenic polypeptide differs from that of the instantly claimed antigen of the amino acid sequence of SEQ ID NO: 3.

Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are anticipated by Cover *et al.* ('132).

21) Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 - Applicants' IDS) (Cover *et al.*, 1992).

The limitation "toxicity" in this rejection is interpreted as encompassing toxicity due to endotoxin. It is noted that the limitation "toxicity" encompasses general toxicity. It is further noted that the transitional recitation "comprising" is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* (1992) disclosed a polypeptide comprising an antigenic N-terminal portion of a cell vacuolating toxin (i.e., cytotoxin) of *Helicobacter pylori* which is recombinantly or synthetically produced and a composition comprising the same in distilled water (see Table III and page 10571, left column). This polypeptide comprising the 23 amino acid-long portion is obtained from the purified toxin antigen and has 100% sequence identity with a 23 amino acid-long contiguous polypeptide portion that stretches between positions 34-56 of the instantly recited SEQ ID NO: 3. The polypeptide has a molecular weight of 87,000, or 972,000 daltons (see page 10573, right column; and page 10574, left column). That the polypeptide comprising the 23 amino acid-long antigenic portion of the prior art, obtained from a purified toxin, is pure enough to be of substantially no endotoxicity, or exhibits substantially reduced contribution to LPS-related toxicity, and that it is long enough to be immunologically identifiable by an *H. pylori*-specific antibody are inherent from the teachings of Cover *et al.* Given that all the structural elements of the instant claims are met by the prior art antigenic polypeptide, the immunological identifiability by an antibody specifically reactive with *H. pylori* cytotoxin and the exhibition of substantially no toxicity, or of substantially reduced toxicity, including cytotoxicity, are viewed as the inherent or intrinsic properties inseparable from the antigenic polypeptide taught by Cover *et al.* (1992).

Furthermore, the term "recombinant" and/or "expressed from ..... nucleotides of SEQ ID NO: 2" in some of the claims represent process limitations. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art antigenic polypeptide differs from that of the instantly claimed antigen of the amino acid sequence of SEQ ID NO: 3.

Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 are anticipated by Cover *et al.* (1992).

Relevant Prior Art

22) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Cover *et al.* (US 5,721,349 and US 6,013,463) disclosed antigenic fragments of a toxic polypeptide of *Helicobacter pylori* that show sequence similarity to the instantly claimed SEQ ID NO: 3 (see entire document).

Remarks

23) Claims 40, 54, 61-65, 72-75, 82-86, 93-96 and 98-101 stand rejected.

24) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

25) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June, 2003

S. DEVI, PH.D.
PRIMARY EXAMINER